Treatment effects of various prescriptions and techniques for fixed orthodontic appliances : A systematic review

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Abstract: PURPOSE: Although several prescriptions and techniques exist for comprehensive fixed appliance treatment, their treatment effects have not yet been adequately assessed in an evidence-based manner. The aim of this systematic review was to assess the therapeutic and adverse effects of various prescriptions or techniques for orthodontic appliances from randomized clinical trials on human patients. METHODS: Eight databases were searched up to July 2016 for randomized trials assessing any orthodontic prescriptions or techniques in human patients. After elimination of duplicate studies, data extraction, and risk of bias assessment according to the Cochrane guidelines, random effects meta-analyses with mean differences (MD) and their 95% confidence intervals (CIs) were performed. RESULTS: Compared to Roth preadjusted appliances, both Begg and modified Begg appliances were associated with statistically significantly worse occlusal outcome assessed with Peer Assessment Review (PAR) scores (1 trial, MD 3.1 points, 95% CI 1.9-4.3 points and 1 trial, MD 2.4 points, 95% CI 1.2-3.6 points, respectively) with low quality of evidence, due to bias and imprecision. Compared to a partially programmed fixed orthodontic appliance, a fully programmed appliance was associated with a statistically significant, but clinically irrelevant increase in treatment duration (1 trial, MD 2.4 months, 95% CI 0.6-4.2 months), supported by high quality of evidence. However, caution is needed in the interpretation of these results as only a limited number of small trials with methodological issues were available. CONCLUSIONS: Based on existing trials, there is limited evidence to support any robust clinical recommendation regarding the prescriptions or techniques for fixed orthodontic appliances. Registration: PROSPERO (CRD42016042727). FUNDING: None.

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Title Page

Treatment effects of the various prescriptions and techniques for the orthodontic fixed appliance: a systematic review

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Running title: Prescriptions for orthodontic appliances

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Conflicts of interest

None.

Keywords: orthodontics, fixed appliances, treatment duration, adverse effects, randomized controlled trials; systematic review, meta-analysis

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Abstract

Purpose Although several prescriptions and techniques exist for comprehensive fixed appliance treatment, their treatment effects have not yet been adequately assessed in an evidence-based manner. Aim of this systematic review was to assess the therapeutic and adverse effects of various prescriptions or techniques for orthodontic appliances from randomized clinical trials on human patients.

Methods Eight databases were searched up to July 2016 for randomized trials assessing any orthodontic prescriptions or techniques in human patients. After duplicate study selection, data extraction, and risk of bias assessment according to the Cochrane guidelines, random-effects meta-analyses of mean differences (MDs) their 95% confidence intervals (CIs) were performed.

Results Compared to Roth pre-adjusted appliances, both Begg and modified Begg appliances were associated with statistically significantly worse occlusal outcome assessed with Peer Assessment Review (PAR) scores (1 trial, MD 3.1 points, 95% CI 1.9-4.3 points and 1 trial, MD 2.4 points, 95% CI 1.2-3.6 points, respectively) with low quality of evidence, due to high of bias and imprecision. Compared to a partially programmed fixed orthodontic appliance, a fully programmed appliance was associated with a statistically significant, but clinically mostly irrelevant increase in treatment duration (1 trial, MD 2.4 monthts, 95% CI 0.6-4.2 months), supported by high quality of bias. However, caution is needed by the interpretation of these results as only a limited number of small trials with methodological issues were available.

Conclusions Based on existing trials, there is limited evidence to support any robust clinical recommendation regarding the prescriptions or techniques for fixed orthodontic appliances.

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Manuscript

Introduction

Rationale

Fixed appliances have become an integral part of comprehensive orthodontic treatment, as a versatile tool for three-dimensional controlled tooth movement. Through the years, a great development in orthodontic appliances and their torque/tip prescription has been seen since the initial appliance designed by E.H. Angle and the introduction of the pre-adjusted ("straight-wire") edgewise appliance by Andrews [4] including the Roth prescription [35], the (MacLaughlin-Bennet-Trevisi) MBT [18] and several other bracket prescriptions or techniques like the Tweed-Merrifield, Begg lightwire, Tip-Edge, bioefficient technique [2, 6, 8, 9, 15, 19, 33, 34, 41, 43]. Among these, the straight-wire concept revolutionized orthodontic treatment with fixed appliances and was founded on the universality of tooth-type shapes and positions, when an exemplary occlusion is present. This enables the incorporation of information about the ideal position of each tooth in the three planes ("prescription") into the brackets that, when correctly prescribed and placed on the tooth surface, enable the correction of malpositioned teeth and dental arches without any bends inserted in the wire.

Over the years, several studies have attempted to assess the treatment effects of existing prescriptions or techniques for orthodontic fixed appliances in terms of occlusal outcome, control of tooth movement, treatment's duration, pain, and discomfort [13, 14, 20, 21, 42]. However, to date, the therapeutic and advert effects of prescriptions or techniques used in comprehensive fixed appliance treatment have not been systematically appraised, according to standard procedures of evidence-based orthodontics [29].

Aim of the present systematic review is to critically assess the available evidence from randomized clinical trials on humans investigating any prescription or technique used for fixed orthodontic appliances and, if possible, to pool evidence from existing trials together in a meta-analysis.

Materials and Methods

Protocol and registration

The protocol for this systematic review was made *a priori* based on the PRISMA-P statement [37], registered in PROSPERO (CRD42016042727), and all *post hoc* changes were appropriately noted. This systematic review is conducted and reported according to Cochrane Handbook [12] and PRISMA statement [16], respectively.

Eligibility criteria

According to the Participants-Intervention-Comparison-Outcome-Study design (PICOS) schema, we included parallel randomized and quasi-randomized prospective controlled trials on human patients comparing any two prescriptions or techniques for fixed orthodontic appliances and assessing therapeutic effects (both effectiveness and efficacy) or adverse effects (Appendix 1). Excluded were non-clinical studies, retrospective studies, animal studies, and studies with partial, self-ligating or lingual appliances.

Information sources and literature search

A total of seven electronic databases (MEDLINE through Pubmed, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, Virtual Health Library, Web of Knowledge, and Scopus) were searched systematically by two authors (SM, SNP) without any limitations for publication year, language or status from inception up to July 21th, 2016 (Appendix 2). Two additional sources (Google Scholar and ISRCTN registry) were manually searched for additional trials or protocols by the same authors. Authors of included trials were contacted for additional missed or ongoing trials. The reference lists and citation lists of the included trials and relevant reviews were manually searched as well.

Study selection and data extraction

Titles identified from the search were screened by one author (SM) with a subsequent duplicate independent checking of their abstracts/full-texts against the eligibility criteria by a second author (SNP), while conflicts were resolved by a third author (TE). Characteristics of included trials and quantitative data were extracted in duplicate by two authors (SM, SNP) using pre-determined and piloted extraction forms. Missing or unclear information was requested by the trials' authors.

Risk of bias in individual trials

The risk of bias of the included trials was assessed using Cochrane's risk of bias tool [12] after initial calibration. A main risk of bias assessment was included in the systematic review pertaining to each trial's primary outcome.

Data synthesis

The Mean Difference (MD) and the Relative Risk (RR) with their corresponding 95% Confidence Interval (CI) were chosen as effect measures for continuous and binary outcomes, respectively. As the outcome of fixed appliance treatment is bound to be affected by characteristics of the used brackets, archwires, and auxiliaries [26-28], a random-effects model according to DerSimonian and Laird [10] was deemed clinically and statistically appropriate for meta-analysis [24]. However, no meta-analyses of two or more studies, assessment of between trial heterogeneity, and additional analyses (subgroup or meta-regression analyses, and sensitivity analyses) could be conducted due to the limited number of included studies. All analyses were run in Stata SE 10.0 (StataCorp, College Station, TX) by one author (SNP). A two-tailed P-value of 0.05 was considered significant for hypothesis-testing.

Risk of bias across studies

The overall quality of evidence (confidence in effect estimates) for each of the main outcomes was rated using the GRADE approach [11]. For this assessment, the risk of bias of each included trial was re-assessed separately at outcome level.

The minimal clinical important, large, and very large effects were conventionally defined [22] as half, one, and two standard deviations, respectively. The standard deviation for an outcome was averaged from control groups of the existing trials. Conventional cut-offs of 1.5, 2.5, and 4.3 were adopted for the RR. Finally, the optimal information size (i.e. required meta-analysis sample size) was calculated for each outcome independently for $\alpha = 5\%$ and $\beta = 20\%$.

Results

Study selection

A total of 580 and 7 papers were identified through electronic (Appendix 2) and manual searches, respectively (Fig. 1). After duplicates' removal and initial screening, 54 papers were assessed for eligibility according to established inclusion criteria and finally 6 papers (5 published and one unpublished) remained for the final analysis [3, 23, 31, 32, 38, 40] (Fig. 1; Appendix 3). In one instance, duplicate publications (one thesis and one journal paper) pertaining to the same trial were grouped together; thus, a total of 5 trials was finally included in the systematic review.

Study characteristics

The characteristics of the trials included can be seen in Table 1. All 5 included studies were parallel randomized clinical trials conducted in 4 different countries. They included a total of 370 patients (with at least 82 male and 103 female patients) with mean ages ranging between 12.3 and 15.3 years. A wide variety of interventions were used to treat different types of malocclusions depending on the eligibility criteria and protocols set in each trial. Roth prescription was compared to either Standard Edgewise (one trial) [32], Begg and Modified Begg appliances (one trial) [38], or to the MBT prescription (one trial) [40]. One unpublished trial [23] compared a Standard Edgewise appliance (Andrews prescription) group to a Tip-Edge appliance. Finally, one study [3] assigned patients to two groups, where maxillary distalization was performed with either three-dimensional bimetric arches (3D-BMDA) or a modified Begg system (MBIDS).

After the start of the active treatment, patients were followed for periods ranging from 8 weeks [40] to 6.5 months [3] and the investigated outcomes included among others treatment duration (3 trials [3,23,31]), chairside time (3 trials [23,31,38]), number of appointments (1 trial [23]), occlusal outcome (3 trials [23,31,38]), space closure (1 trial [31]), radiographic outcomes of tooth position/inclination (5 trials [3,23,31,38,40]), oral health (1 trial [31]), cost effectiveness (1 trial [23]), root resorption (1 trial [31]), and patient discomfort (1 trial [31]) (Table 1). The corresponding authors of included trials were contacted in several instances to request additional data. However, apart from one unpublished study [23], where the corresponding author provided a draft of the unpublished paper, no additional data could be retrieved.

Risk of bias within studies

A summary of the risk of bias for all studies can be seen in Fig. 2. The detailed risk of bias assessment for the included trials can be found in Appendix 4. High risk of bias was found in three trials (60%) for at least one bias domain. The most problematic domains were the blinding of outcome assessment (problematic in 60% of the trials), followed by incomplete outcome data (found in 20% of the trials).

Results of individual studies and data synthesis

The retrieved results for all reported outcomes of all individual studies are quantitatively represented in Table 2. Substantial differences in the implemented interventions, participants' characteristics, observational periods and investigated outcomes among studies were observed, making them incompatible. Thus, no meta-analysis was attempted.

The statistically significant (P<0.05) effects reported from the included studies can be summarized as follows. Roth appliance was associated with a lower Peer Assessment Rating (PAR) score (better occlusal outcome), but also an increase in total chairside time compared to Begg appliance. Roth appliance was also associated with a lower PAR score (better occlusal outcome) compared to a modified Begg appliance. Also significant short-term differences in the inclination of the upper and lower incisors and the upper canines were found between Roth and MBT appliances. When a fully programmed fixed orthodontic appliance was compared to a partially programmed one, a statistically significant, but clinically irrelevant, increase in treatment duration by 0.2 month was reported. Finally, several cephalometric differences were found between the 3D-BMDA and the modified Begg distalization technique, but these were only minor and short-term.

Risk of bias across studies – GRADE assessment

The outcomes that were selected for assessment in the GRADE analysis were total treatment duration or chairtime, occlusal outcome (PAR score), upper incisor inclination, lower incisor inclination, and root resorption.

A. Comparison of Roth versus Begg and modified Begg fixed orthodontic appliances

Compared to the Roth appliance, use of the Begg appliance could probably decrease total chairtime, while the time saving with the use of a modified Begg appliance was statistically insignificant (moderate quality evidence for both). Additionally, based on low quality evidence use of either the Begg or the modified Begg appliance may deteriorate slightly the final occlusal outcome of treatment. Finally, no considerable differences in the inclination of the upper or lower incisors were found between Roth, Begg, and modified Begg appliances (low quality of evidence). The main reasons for downgrading the quality of existing evidence were risk of bias due to methodological inadequacies and imprecision due to the small sample of the included trial.

B. Comparison of a fully versus a partially programmed fixed orthodontic appliance.

Based on existing high quality evidence coming from a single trial, the use of a fully-programmed appliance slightly increases treatment duration (by about 2.4 months) compared to a partially-programmed appliance, but seems to have little or no effect on occlusal outcome, incisor inclination, or the prevalence of root resorption after treatment (Table 4).

Discussion

Summary of evidence

The present systematic review included five parallel randomized clinical trials and a total of 370 patients. Interestingly, although most of the prescriptions/techniques in question exist for several decades, there is a considerable lack of clinical evidence regarding both their therapeutic and adverse effects that could enable the formulation of robust clinical recommendations for their use. This is mainly due to the small number of trials with limited sample sizes that were identified, which implemented different protocols and assessed diverse outcomes, making overall data synthesis difficult.

Nevertheless, data analysis was considered feasible in the following two instances; in the comparison of comprehensive orthodontic treatment with Roth versus treatment with Begg or modified Begg appliance and in the comparison of a fully versus a partially programmed appliance where clinically important outcomes were reported. Use of a Begg appliance was associated with reduced chairside time compared to the use of a Roth appliance, which might imply more efficient treatment. On the other hand, the Begg appliance was associated with a worse occlusal outcome at the end of treatment as indicated by PAR, when compared to Roth. Therefore, no clear recommendations about treatment effectiveness with Roth or Begg appliances can be done. Additionally, these findings should be interpreted with caution, due to the observed moderate to high risk of bias and imprecision.

As for the outcomes obtained with the use of a fully programmed appliance (straight wire concept) compared to a partially programmed one (conventional full edgewise concept) [32], limited high quality evidence indicates that no considerable differences exist in the occlusal outcome, the final inclination of the upper or lower incisors, or the prevalence of root resorption after treatment. The only statistically significant difference was a slight decrease in treatment duration with the partially programmed appliance (2.4 months), which is probably irrelevant to the clinician. Therefore, both appliance types could, theoretically, be equally effective in treating malocclusions and appliance choice still remains, mainly, with the personal preference of the clinician.

Beyond the aforementioned findings, a considerable amount of retrospective studies concerning the clinical assessment of various prescriptions and techniques for fixed orthodontic appliances is also available in the literature [13, 14, 20, 21, 42]. In the study of Kattner and Schneider [14] no differences in the ideal tooth relationship index were found when study models of patients treated with a Roth prescription pre-adjusted edgewise appliance were compared to those of patients treated with a standard edgewise appliance. In addition, Ugur and Yukay [42] found no

differences in torque values between cases treated with standard edgewise and Roth prescription appliances by implementing an accurate method for the evaluation of faciolingual tooth inclination, as described by Andrews [4].

Comparisons between various techniques have been also performed in previous retrospective clinical studies, which were excluded from the present review due to their high risk of bias. Jain et al. [13] retrospectively assessed the occlusal outcome with the Objective Grading System (OGS) of the American Board of Orthodontists (ABO) after treatment with a Roth or an MBT appliance. They reported that the use of the MBT appliance was associated with a significantly better occlusal outcome than the Roth appliance (MD -2.7 OGS points; 95% -1.0 to -4.3 OGS points; $P<0.05$). However, if we look at the baseline malocclusion severity of the two groups, we can see that the MBT group included patients with significantly "easier" malocclusions than the Roth group, as assessed with the ABO Discrepancy Index (DI) (MD -3.8 points; 95% CI -0.4 to -7.2 points; $P<0.05$). This can be better illustrated, if we divide the mean OGS score with the mean DI score in each group, which would result in 1.49 and 1.74 for the Roth and MBT appliance, respectively. This means that given similar conditions, the Roth appliance is more efficient than the MBT appliance (both the OGS and the DI are scored negatively, meaning that less is better). Bias by confounding, as can be seen in this example, is just one of the several inherent limitations of retrospective study designs [30], which make them potentially inappropriate to base clinical recommendations upon. Additionally, Moesi et al. [21] found that bracket prescription had no effect on the subjective aesthetic outcome after treatment with either a Roth or MBT appliances. Furthermore, Mittal et al. [20] reported several tooth alignment outcomes after treatment with Roth or MBT appliances.

As far as straightwire versus Standard Edgewise appliances are concerned, Soltani et al. [39] reported that treatment with an MBT straightwire or a Standard Edgewise appliance resulted in similar occlusal outcomes (mean OGS of 20.0 and 20.4, respectively), but treatment with MBT straightwire appliance was slightly shorter than with the Standard Edgewise appliance (24.0 and 26.0 months, respectively). In the study of Beg [5] a Roth straightwire appliance was compared with a Standard Edgewise appliance in the treatment of Class I malocclusion. Re-analysis of the provided raw data with multivariable regression indicated that Roth appliances were associated with slightly greater effectiveness (PAR 1.49 points more) and slightly greater treatment duration (2.69 months more) compared to Standard Edgewise appliance, although both were statistically non-significant (P values of 0.104 and 0.180, respectively). Additionally, Wu et al [44] reported that MBT appliances were better to control the mesial inclination of molars, the vertical movement, and torque of anterior teeth during treatment than Standard Edgewise appliances. Mavragani et al [17] systematically compared straightwire and Standard Edgewise appliances, both in 0.018-inch

slot, in extraction treatment and found that straightwire appliances were associated with statistically significant less root resorption of the incisors than Standard Edgewise appliances, which was attributed to more efficient force control with this technique. Finally, Akhoundi et al [1] reported that significantly more patients treated with straightwire appliances demonstrated canine guidance on laterotrusion and mutually protected occlusion post-treatment compared to patients treated with Standard Edgewise appliances. However, these results should be interpreted with caution, since they originate from retrospective studies that inherently are in high risk of bias.

Strengths and limitations

This systematic review provides a succinct summary of existing evidence with its main strengths being it's *a priori* registration in PROSPERO [71], the extensive unrestricted literature search, the inclusion of unpublished data, the use of robust methodology pertaining to the qualitative and quantitative synthesis of data [25], the exclusion of biased study designs [30], transparent reporting of quantitative data for all outcomes from included studies, assessment of the quality of evidence with the GRADE approach [11], and the clear reporting of any deviations from the review's protocol (Appendix 8). However, this systematic review also has some limitations, like the limited number of included trials, which precluded the assessments of heterogeneity, subgroup analyses, small-study effects, and reporting biases for most of the outcomes. Although this could not be formally assessed as only a limited number of studies were, the risk of publication bias might be considered minimal due to the extensive literature search, which was not limited to publications in scientific journals. Furthermore, despite our efforts, no response was obtained from most contacted authors, apart from one author that provided an unpublished study [23].

Recommendations for clinical practice

There is insufficient evidence at present to make robust recommendations about any prescriptions or techniques for the fixed orthodontic appliance in terms of therapeutic or adverse effects. Existing evidence indicates that only minor differences can be directly attributed to the choice of prescription/technique, which are clinically irrelevant and our confidence in these estimates is very poor.

Recommendations for further research

Parallel randomized clinical trials or well-designed prospective trials with blinded outcome assessment are needed in order to form robust clinical recommendations. These should ideally be carried out according to the Consolidated

Standards of Reporting Trials (CONSORT) statement [36] and adequately report on objective outcomes of treatment effectiveness and efficiency. These could include several therapeutic effects (like treatment duration, occlusal outcome with OGS, patient satisfaction / quality of life, and relapse) or adverse effects (including root resorption, white spot lesions, gingival recessions, oral pain, oral discomfort, functional impairment, and cost of treatment) so that reliable conclusions can be reached.

Conclusions

The present systematic review suggests that there is currently insufficient data to support the evidence-based clinical use of any particular prescription or technique for fixed orthodontic appliances over another in terms of efficiency, effectiveness, or side-effects.

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Figure legends

Fig. 1 Flowdiagram for the identification and selection of studies in this systematic review.

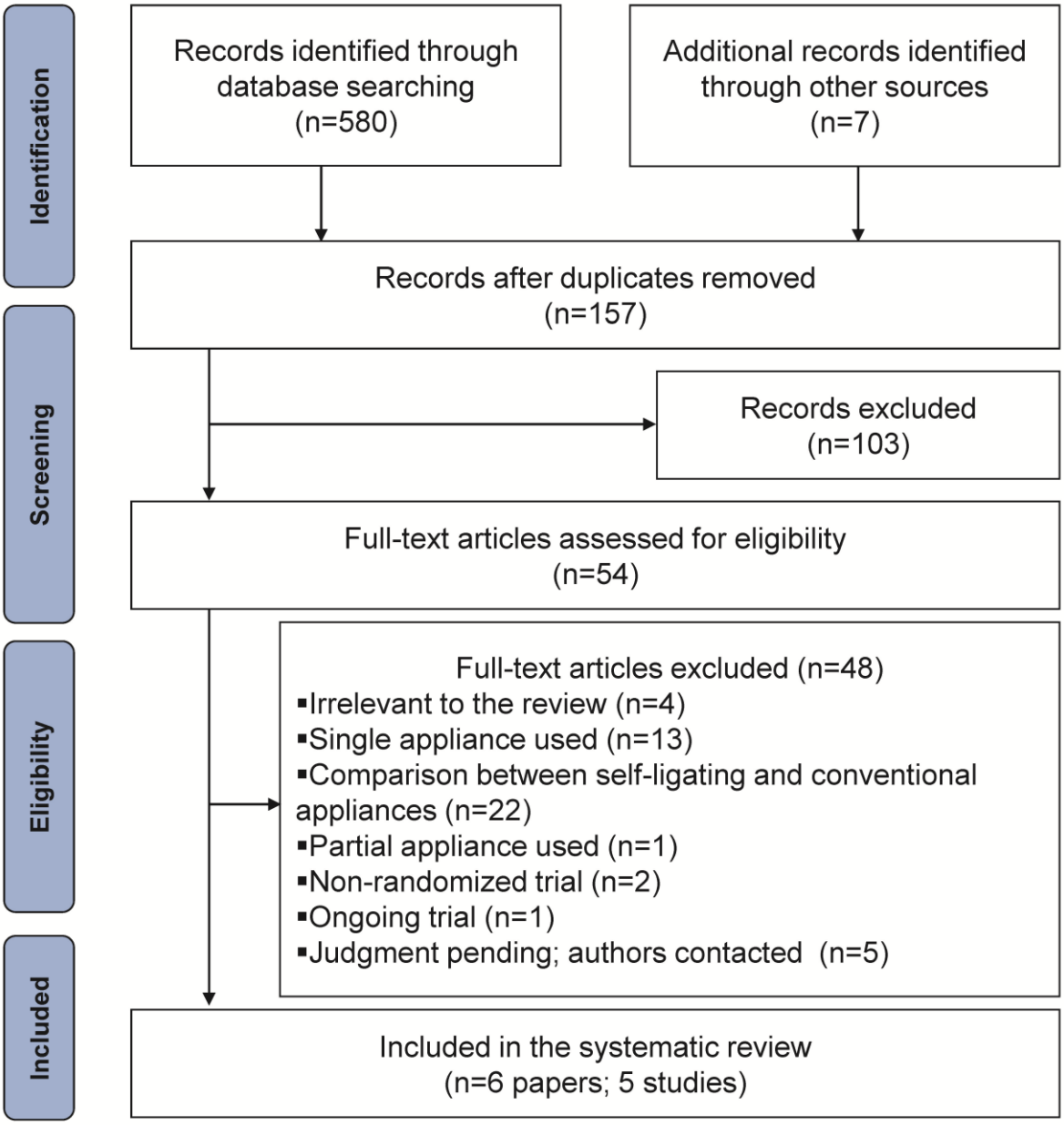
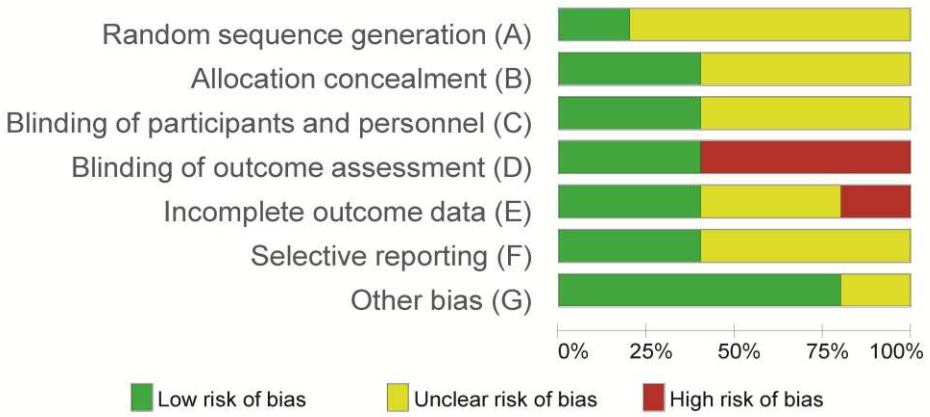
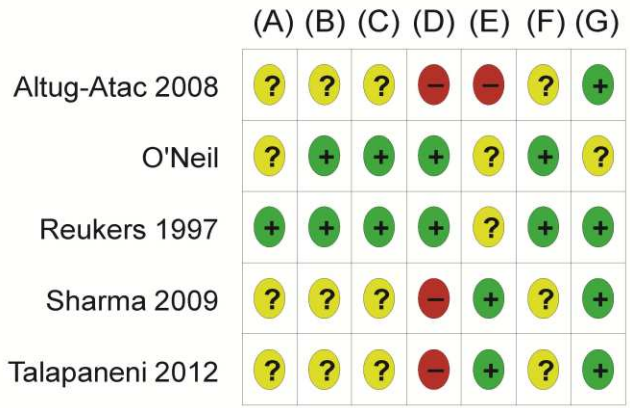


Fig. 2 Summary of the risk of bias of the trials included in this systematic review.





Tables

Table 1. Characteristics of the included trials.

Nr	Trial	Design	Patients (M/F)	Mean age (yr)	Intervention	Follow-up	Outcome	Conflict of interest
1	Altug-Atac 2008	RCT_{PAR}; University; Turkey	G1: 21 (9/12) G2:17 (3/14)	G1: 14.7 G2: 14.4	G1: 3D-BMDA G2: MBIDS	G1: 3.4 mos G2: 6.5 mos	(Clin/LCeph) Tx duration; Max molar distalization; Mnd incisor proclination; Mnd anchorage loss	Not declared; University funding
2	O'Neil (unpublished)	RCT_{PAR}; Hospital; UK	G1: 38 (NR) G2: 35 (NR)	NR	G1: Standard edgewise G2: Tipp-Edge	Tx completion	(Clin/Model/LCeph) Tx duration; Chairside time; Number of attended and missed appointments; various cephalometric outcomes; Occlusal outcome (PAR); appliance cost; adverse effects	Not declared; company donation
3	Reukers 1997; 1998	Multi-center RCT_{PAR}; University; Netherlands	G1/G2: 149 (64/85)	G1/G2: 12.3	G1: Roth prescription G2: Standard edgewise	G1: 1.8 yrs G2: 1.6 yrs	(Clin/Photo/Model/Rad./Quest.) Tx duration; Chairside time; GI; PI; Occlusal outcome (CPITN, PAR, ITRI); Extraction space closure; Angulation of upper anterior teeth; Root resorption; Patient discomfort	Not declared; company funding
4	Sharma 2009	RCT_{PAR}; AFDC; New Delhi	G1-G3: 90 (NR)	Matched	G1: Modified Begg G2: Begg G3: Roth prescription	Tx completion	(Clin/Rad.) Correction of bimaxillary dentoalveolar protrusion; PAR; Chairside time	Not declared; grant funding
5	Talapaneni 2012	RCT_{PAR}; Dental College/Hospital; India	G1: 15 (9/6) G2: 5 (7/8)	G1: 14.9 G2: 15.3	G1: MBT prescription; G2: ROTH prescription	8 wks	(Rad./Photo.) Inclination of upper anterior teeth; mesial movement of Max molar	Not declared

M, male; F, female; yr, year; RCT_{PAR}, parallel randomized controlled trial; FPA, fully programmed edgewise appliance; PFA, partly programmed edgewise appliance; PAR, Peer Assessment Rating; CPITN, The Community Periodontal Index of Treatment Needs; GI, Gingival Index; PI, Plaque Index; ITRI, Ideal Tooth Relationship Index; AFDC, Armed Forces Dental Clinic; PEA, Pre-adjusted edgewise appliance; NR, not reported; G, group; 3D-BMDA, Three-dimensional bimetric maxillary distalization arches; MBIDS, modified Begg intraoral distalization system; MBT, McLaughlin-Bennett-Trevisi.

Table 2. Results of the included studies for all reported outcomes.

Nr	T	Comparison	Mos	O	Variable	MD (95% CI)*	P*	Clinical relevance†
1	T1	3D-BMDA vs MBIDS	3.4-6.5	O1	SNA (°)	-0.15 (-0.69,0.39)	0.584	-
2	T1	3D-BMDA v MBIDS	3.4-6.5	O1	A-max.VR (mm)	**-0.88 (-1.58,-0.18)**	**0.014**	Yes
3	T1	3D-BMDA v MBIDS	3.4-6.5	O1	SN-PP (°)	0.32 (-0.32,0.96)	0.328	-
4	T1	3D-BMDA v MBIDS	3.4-6.5	O1	Co-A (mm)	0.27 (-1.13,1.67)	0.705	-
5	T1	3D-BMDA v MBIDS	3.4-6.5	O1	N-ANS (mm)	-0.20 (-0.77,0.37)	0.492	-
6	T1	3D-BMDA v MBIDS	3.4-6.5	O1	ANS- HR (mm)	-0.14 (-0.70,0.37)	0.624	-
7	T1	3D-BMDA v MBIDS	3.4-6.5	O1	PNS- HR (mm)	-0.31 (-0.81,0.19)	0.224	-
8	T1	3D-BMDA v MBIDS	3.4-6.5	O1	SNB (°)	0.15 (-0.45,0.75)	0.621	-
9	T1	3D-BMDA v MBIDS	3.4-6.5	O1	B-mand.VR (mm)	-0.31 (-1.76,1.14)	0.675	-
10	T1	3D-BMDA v MBIDS	3.4-6.5	O1	SN/GoGn (°)	**-0.80 (-1.51,-0.09)**	**0.027**	No
11	T1	3D-BMDA v MBIDS	3.4-6.5	O1	Co-Gn (mm)	-0.31 (-1.70,1.08)	0.663	-
12	T1	3D-BMDA v MBIDS	3.4-6.5	O1	Co-Go (mm)	0.22 (-1.05,1.49)	0.735	-
13	T1	3D-BMDA v MBIDS	3.4-6.5	O1	N-Me (mm)	**-1.72 (-2.61,-0.83)**	**<0.001**	Yes
14	T1	3D-BMDA v MBIDS	3.4-6.5	O1	S-Go (mm)	-0.62 (-1.49,0.25)	0.162	-
15	T1	3D-BMDA v MBIDS	3.4-6.5	O1	ANB (°)	-0.20 (-0.80,0.40)	0.512	-
16	T1	3D-BMDA v MBIDS	3.4-6.5	O1	SN-OP (°)	**-3.56 (-5.48,-1.65)**	**<0.001**	Yes
17	T1	3D-BMDA v MBIDS	3.4-6.5	O1	ANS-Me (mm)	**-1.29 (-2.22,-0.36)**	**0.007**	No
18	T1	3D-BMDA v MBIDS	3.4-6.5	O1	1s-NL (°)	1.33 (-2.25,4.91)	0.467	-
19	T1	3D-BMDA v MBIDS	3.4-6.5	O1	6s-NL (°)	0.10 (-3.37,3.57)	0.955	-
20	T1	3D-BMDA v MBIDS	3.4-6.5	O1	7s-NL (°)	-2.99 (-6.10,0.12)	0.060	-
21	T1	3D-BMDA v MBIDS	3.4-6.5	O1	1i-ML (°)	-2.39 (-5.55,0.77)	0.139	-
22	T1	3D-BMDA v MBIDS	3.4-6.5	O1	6i-ML (°)	**4.33 (1.19,7.47)**	**0.007**	No
23	T1	3D-BMDA v MBIDS	3.4-6.5	O1	1s-Svert (mm)	-0.39 (-4.68,3.90)	0.859	-
24	T1	3D-BMDA v MBIDS	3.4-6.5	O1	6s-Svert (mm)	-0.28 (-1.76,1.20)	0.710	-
25	T1	3D-BMDA v MBIDS	3.4-6.5	O1	6s-Svert per month (mm)	**-0.57 (-0.99,-0.15)**	**0.008**	No
26	T1	3D-BMDA v MBIDS	3.4-6.5	O1	7s-Svert (mm)	0.36 (-2.29,3.01)	0.790	-
27	T1	3D-BMDA v MBIDS	3.4-6.5	O1	1s-NL (mm)	-0.57 (-1.49,0.35)	0.227	-
28	T1	3D-BMDA v MBIDS	3.4-6.5	O1	6s-NL (mm)	**0.53 (0.03,1.03)**	**0.039**	No
29	T1	3D-BMDA v MBIDS	3.4-6.5	O1	7s-NL (mm)	**0.68 (0.15,1.21)**	**0.012**	No
30	T1	3D-BMDA v MBIDS	3.4-6.5	O1	1i-Svert (mm)	-1.58 (-4.59,1.43)	0.303	-
31	T1	3D-BMDA v MBIDS	3.4-6.5	O1	6i-Svert (mm)	0.76 (-2.06,3.58)	0.597	-
32	T1	3D-BMDA v MBIDS	3.4-6.5	O1	1s-ML (mm)	1.59 (-1.43,4.61)	0.303	-
33	T1	3D-BMDA v MBIDS	3.4-6.5	O1	6s-ML (mm)	-0.75 (-2.95,1.45)	0.505	-
34	T1	3D-BMDA v MBIDS	3.4-6.5	O1	Overjet (mm)	-0.43 (-1.77,0.91)	0.529	-
35	T1	3D-BMDA v MBIDS	3.4-6.5	O1	Overbite (mm)	**2.63 (1.34,3.92)**	**<0.001**	Yes
36	T1	3D-BMDA v MBIDS	3.4-6.5	O1	Ls–Steiner (mm)	-0.33 (-1.21,0.55)	0.461	-
37	T1	3D-BMDA v MBIDS	3.4-6.5	O1	Li–Steiner (mm)	**-1.09 (-1.86,-0.32)**	**0.005**	No
38	T2	FPA vs PPA	Tx end	O2	Tx duration (mos)	**0.20 (0.05,0.35)**	**0.009**	No
39	T2	FPA vs PPA	Tx end	O3	Degree of root resorption	0.70 (-2.85,4.25)	0.699	-
40	T2	FPA vs PPA	Tx end	O3	% prevalence of root resorption	[1.36 (0.93,2.00)]	[0.120]	-
41	T2	FPA vs PPA	4.0	O4	Oral hygiene aids use	0.10 (-0.08,0.28)	0.281	-
42	T2	FPA vs PPA	10.0	O4	Oral hygiene aids use	0.10 (-0.10,0.30)	0.317	-
43	T2	FPA vs PPA	Tx end	O4	Oral hygiene aids use	0.00 (-0.25,0.25)	1.000	-
44	T2	FPA vs PPA	Tx end	O5	% PAR score change	-0.40 (-4.72,3.92)	0.856	-
45	T2	FPA vs PPA	Tx end	O5	Perfect PAR score (maxillary front)	[1.04 (0.85,1.27)]	[0.690]	-
46	T2	FPA vs PPA	Tx end	O5	Perfect PAR score (mandibular front)	[0.91 (0.78,1.07)]	[0.270]	-
47	T2	FPA vs PPA	Tx end	O5	Perfect PAR score (occlusion)	NE	NE	-
48	T2	FPA vs PPA	Tx end	O5	Perfect PAR score (overjet)	[1.00 (0.86,1.16)]	[1.000]	-

49	T2	FPA vs PPA	Tx end	O5	Perfect PAR score (overbite)	[1.03 (0.95,1.12)]	[0.467]	-
50	T2	FPA vs PPA	Tx end	O5	Perfect PAR score (midline)	[1.03 (0.96,1.11)]	0.405]	-
51	T2	FPA vs PPA	Tx end	O5	Ideal Tooth Relationship Index score (maxilla & mandible)	2.80 (-12.18,17.78)	0.714	-
52	T2	FPA vs PPA	Tx end	O5	Ideal Tooth Relationship Index score (maxilla)	9.60 (-2.01,21.21)	0.105	-
53	T2	FPA vs PPA	Tx end	O5	Ideal Tooth Relationship Index score (mandible)	-11.50 (-25.30,2.30)	0.102	-
54	T2	FPA vs PPA	Tx end	O6	1s-NL (°)	-2.00 (-4.59,0.59)	0.131	-
55	T2	FPA vs PPA	Tx end	O6	1s-OP (°)	1.00 (-1.05,3.05)	0.339	-
56	T2	FPA vs PPA	Tx end	O6	1i-OP (°)	-1.00 (-3.59,1.59)	0.450	-
57	T2	FPA vs PPA	Tx end	O6	1i-ML (°)	3.00 (-1.09,7.09)	0.150	-
58	T2	FPA vs PPA	Tx end	O6	1s-1i (°)	0.00 (-4.08,4.08)	1.000	-
59	T3	PEA vs Begg	Tx end	O1	SNA (°)	0.06 (-1.59,1.71)	0.943	-
60	T3	PEA vs Begg	Tx end	O1	SNB (°)	-0.23 (-1.77,1.31)	0.770	-
61	T3	PEA vs Begg	Tx end	O1	ANB (°)	0.10 (-1.63,1.83)	0.910	-
62	T3	PEA vs Begg	Tx end	O1	1i-ML (°)	1.00 (-3.20,5.20)	0.641	-
63	T3	PEA vs Begg	Tx end	O1	1s-SN (°)	0.00 (-5.11,5.11)	1.000	-
64	T3	PEA vs Begg	Tx end	O1	SN-OP (°)	0.20 (-3.61,4.01)	0.918	-
65	T3	PEA vs Begg	Tx end	O1	SN-ML (°)	-1.50 (-5.22,2.22)	0.429	-
66	T3	PEA vs Begg	Tx end	O5	PAR (final)	**3.11 (1.90,4.33)**	**<0.001**	No
67	T3	PEA vs Begg	Tx end	O2	Tx duration (total chairtime in minutes)	**-65.03 (-92.51,-37.56)**	**<0.001**	Yes
68	T3	PEA vs mod Begg	Tx end	O1	SNA (°)	1.06 (-0.51,2.63)	0.187	-
69	T3	PEA vs mod Begg	Tx end	O1	SNB (°)	-0.23 (-1.87,1.41)	0.783	-
70	T3	PEA vs mod Begg	Tx end	O1	ANB (°)	0.10 (-1.02,1.22)	0.861	-
71	T3	PEA vs mod Begg	Tx end	O1	1i-ML (°)	2.00 (-1.93,5.93)	0.318	-
72	T3	PEA vs mod Begg	Tx end	O1	1s-SN (°)	0.00 (-4.90,4.90)	1.000	-
73	T3	PEA vs mod Begg	Tx end	O1	SN-OP (°)	0.20 (-3.21,3.61)	0.909	-
74	T3	PEA vs mod Begg	Tx end	O1	SN-ML (°)	0.50 (-3.35,4.35)	0.799	-
75	T3	PEA vs mod Begg	Tx end	O5	PAR (final)	**2.36 (1.15,3.58)**	**<0.001**	No
76	T3	PEA vs mod Begg	Tx end	O2	Tx duration (total chairtime in minutes)	14.57 (-12.91,42.05)	0.299	-
77	T4	MBT vs Roth	2.0	O1	1s-Sperp (mm)	**-2.67 (-3.54,-1.80)**	**<0.001**	Yes
78	T4	MBT vs Roth	2.0	O1	1i-Sperp (mm)	**-2.34 (-3.24,-1.44)**	**<0.001**	Yes
79	T4	MBT vs Roth	2.0	O1	6s-Sperp (mm)	-1.33 (-2.72,0.06)	0.061	-
80	T4	MBT vs Roth	2.0	O1	6i-Sperp (mm)	NE	NE	-
81	T4	MBT vs Roth	2.0	O1	1s-NL (mm)	-0.03 (-0.43,0.37)	0.884	-
82	T4	MBT vs Roth	2.0	O1	1i-ML (mm)	-0.06 (-0.54,0.42)	0.806	-
83	T4	MBT vs Roth	2.0	O1	3s-SN (°)	**2.67 (0.59,4.75)**	**0.012**	No

T-Trial; T1-Altug-Atac 2008; T2-Reukers 1997; T3-Sharma 2009; T4-Talapaneni 2012; Mos, months; O-Outcome; O1-cephalometric analysis (increment post-pre) ; O2-clinical assessment; O3-periapical radiograph; O4-questionnaire; O5-model analysis; O6-cephalometric analysis (final values); MD, mean difference; CI, confidence interval; 3D-BMDA, three-dimensional bimetric maxillary distalization arches; MBIDS, modified Begg intraoral distalization system; NE, not estimable; PAR, peer assessment rating; Tx, treatment; FPA, fully preadjusted appliance; PPA, partly preadjusted appliance; PEA, preadjusted appliance; MBT, MacLaughlin Bennet Trevisi.

* Values in brackets indicate relative risks with the corresponding 95% confidence intervals for binary outcomes. Bold indicates significant at the 5% level.

†Judged naively as effects larger than at least one SD of the control group.

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Table 3. Summary of Findings table regarding the comparison of Roth versus Begg and modified Begg fixed orthodontic appliances.

Outcomes, no of participants (studies)	Roth vs	With Roth	With Begg/ mod. Begg	Difference	Quality of the Evidence (GRADE)	What happens
Total chairtime (in minutes) 20 patients (1 study)	Begg	Mean chairtime of 304.0 minutes	-	65.0 minutes less (95% CI: 37.6 to 92.5 less)	⊕⊕⊕⊖ moderate due to risk of bias	Probably decreases total chairtime
Total chairtime (in minutes) 20 patients (1 study)	mod. Begg		-	14.6 minutes more (95% CI: 12.9 less to 42.1 more)	⊕⊕⊕⊖ moderate due to risk of bias	Little or no difference
Occlusal outcome (final PAR) 20 patients (1 study)	Begg	Mean PAR of 6.6 points	-	3.1 points more (95% CI: 1.9 to 4.3 more)	⊕⊕⊖⊖ low due to risk of bias and imprecision	May increase PAR score
Occlusal outcome (final PAR) 20 patients (1 study)	mod. Begg		-	2.4 points more (95% CI: 1.2 to 3.6 more)	⊕⊕⊖⊖ low due to risk of bias and imprecision	May increase PAR score
Upper incisor inclination (1s-SN change in °) 20 patients (1 study)	Begg	Mean inclination change of -15.0°	-	0.0° difference (95% CI: 5.1 less to 5.1 more)	⊕⊕⊖⊖ low due to risk of bias and imprecision	Little or no difference
Upper incisor inclination (1s-SN change in °) 20 patients (1 study)	mod. Begg		-	0.0° difference (95% CI: 4.9 less to 4.9 more)	⊕⊕⊖⊖ low due to risk of bias and imprecision	Little or no difference
Lower incisor inclination (1s-SN change in °) 20 patients (1 study)	Begg	Mean inclination change of -4.0°	-	1.0° more (95% CI: 3.2 less to 5.2 more)	⊕⊕⊖⊖ low due to risk of bias and imprecision	Little or no difference
Lower incisor inclination (1s-SN change in °) 20 patients (1 study)	mod. Begg		-	2.0° more (95% CI: 1.9 less to 5.9 more)	⊕⊕⊖⊖ low due to risk of bias and imprecision	Little or no difference

Abbreviations: CI, Confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PAR, peer assessment rating.
Patient or population: patients in need of comprehensive fixed appliance treatment.
Settings: university clinic.
Intervention: Begg or modified Begg technique.
Comparison: Roth technique.

Table 4. Summary of Findings table regarding the comparison of a fully versus a partially programmed fixed orthodontic appliance.

		Anticipated absolute effects (95% CI)				
Outcomes, no of participants (studies)	Relative effect (95% CI)	With PPA	With FPA	Difference	Quality of the Evidence (GRADE)	What happens
Tx duration (in months) 140 patients (1 study)	-	Mean Tx duration of 19.2 months	-	2.4 months more (95% CI: 0.6 to 4.2 months more)	⊕⊕⊕⊕ high	Slighlty increases Tx duration
Occlusal outcome (% reduction of initial PAR score) 134 patients (1 study)	-	Mean reduction of 85.2 %	-	0.4% less (95% CI: 4.7% less to 3.9% more)	⊕⊕⊕⊕ high	Little or no difference
Upper incisor inclination (final 1s-NL in °) 112 patients (1 study)	-	Mean inclination of 111.0°	-	2.0° less (95% CI: 4.6° less to 0.6° more)	⊕⊕⊕⊕ high	Little or no difference
Lower incisor inclination (final 1i-ML in °) 112 patients (1 study)	-	Mean inclination of 99.0°	-	3.0° more (95% CI: 1.1° less to 7.1° more)	⊕⊕⊕⊕ high	Little or no difference
Prevalence of root resorption 61 patients (1 study)	RR 1.36 (0.93,2.00)	55%	74.8% (51.2 to 110%)	19.8% more patients (3.9% fewer to 55.0% more)	⊕⊕⊕⊕ high	Little or no difference

Abbreviations: CI, Confidence interval; PPA, partly programmed appliance; FPA, fully programmed appliance; GRADE, Grading of Recommendations Assessment, Development and Evaluation; Tx, treatment; MD, mean difference; PAR, peer assessment rating; RR, risk ratio.
Patient or population: patients in need of comprehensive fixed appliance treatment.
Settings: university clinic.
Intervention: FPA.
Comparison: PPA.

Appendix

Treatment effects of the various prescriptions and techniques for the orthodontic fixed appliance: a systematic review

Appendix 1. Inclusion/exclusion criteria for this systematic review.

Domain	Inclusion	Exclusion
Participants	▪ Human patients of any age/sex/ethnicity with any type of malocclusion	▪ Animal studies
Interventions	▪ Any prescription or technique for comprehensive fixed appliance treatment	▪ Trials with partial appliances ▪ Trials with self-ligating or lingual appliances
Comparisons	▪ No treatment ▪ Any other kind of treatment	-
Outcome	▪ Treatment duration ▪ Occlusal outcome ▪ Prevalence / severity of root resorption ▪ Torque/inclination of the anterior teeth after treatment ▪ Sagittal anchorage loss of the first molar during space closure ▪ Stability of the treatment results after debonding.	-
Study design	▪ Randomized controlled trials (parallel) ▪ Quasi-randomized controlled trials (parallel)	▪ Clustered study designs with partial appliances ▪ Non-randomized prospective or retrospective studies ▪ Case reports/ case series ▪ Non-clinical studies (in vitro, ex vivo, in silico, etc) ▪ Systematic reviews (after checked for studies)

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Appendix 2. Literature databases searched with search strategy and yield (last search July 21, 2016).

Database	Search Strategy	Limitations	Hits
MEDLINE	orthodon* AND (prescription* OR technique* OR appliance* OR bracket*) AND (Alexander OR Andrews OR Begg OR Bench OR Bennett OR Bioefficient OR "Bioefficient" OR Bioprogressive OR "Bio-progressive" OR Burstone OR Celtin OR "Combination Anchorage" OR Creekmore OR Damon OR Edgewise OR "fully-prescribed" OR Hanson OR Hasund OR Hilgers OR lightwire OR "light-wire" OR MBT OR McLaughin OR Merrifield OR Orthos OR "pre-programmed" OR Ricketts OR Roncone OR Roth OR "Standard Edgewise" OR "Straight wire" OR Straightwire OR "Tip-Edge" OR Trevisi OR Tweed OR "Tweed/Merrifield" OR "Variable Prescription Orthodontics") NOT ("bond strength" OR toothbrush OR primer OR "in vitro" OR pulp*) AND (random* OR blind*)	Clinical Trial/Comparative Study/Randomized Controlled Trial Humans	91
CDSR	same		0
DARE	same		0
CENTRAL	same		51
VHL	orthodon* AND (prescription* OR technique* OR appliance* OR bracket*) AND (Alexander OR Andrews OR Begg OR Bench OR Bennett OR Bioefficient OR "Bioefficient" OR Bioprogressive OR "Bio-progressive" OR Burstone OR Celtin OR "Combination Anchorage" OR Creekmore OR Damon OR Edgewise OR "fully-prescribed" OR Hanson OR Hasund OR Hilgers OR lightwire OR "light-wire" OR MBT OR McLaughin OR Merrifield OR Orthos OR "pre-programmed" OR Ricketts OR Roncone OR Roth OR "Standard Edgewise" OR "Straight wire" OR Straightwire OR "Tip-Edge" OR Trevisi OR Tweed OR "Tweed/Merrifield" OR "Variable Prescription Orthodontics") NOT ("bond strength" OR toothbrush OR primer OR "in vitro" OR pulp*) AND (random* OR blind*)		1
WoK	orthodon* AND (prescription* OR technique* OR appliance* OR bracket*) AND (Alexander OR Andrews OR Begg OR Bench OR Bennett OR Bioefficient OR "Bioefficient" OR Bioprogressive OR "Bio-progressive" OR Burstone OR Celtin OR "Combination Anchorage" OR Creekmore OR Damon OR Edgewise OR "fully-prescribed" OR Hanson OR Hasund OR Hilgers OR lightwire OR "light-wire" OR MBT OR McLaughin OR Merrifield OR Orthos OR "pre-programmed" OR Ricketts OR Roncone OR Roth OR "Standard Edgewise" OR "Straight wire" OR Straightwire OR "Tip-Edge" OR Trevisi OR Tweed OR "Tweed/Merrifield" OR "Variable Prescription Orthodontics") NOT ("bond strength" OR toothbrush OR primer OR "in vitro" OR pulp*) AND (random* OR blind*)	DENTISTRY ORAL SURGERY MEDICINE	46
Scopus	(TITLE-ABS-KEY (orthodon*) AND TITLE-ABS-KEY (prescription* OR technique* OR appliance* OR bracket*) AND TITLE-ABS-KEY (alexander OR andrews OR begg OR bench OR bennett OR bioefficient OR "Bioefficient" OR bioprogressive OR "Bio-progressive" OR burstone OR celtin OR "Combination Anchorage" OR creekmore OR damon OR edgewise OR "fully-prescribed" OR hanson OR hasund OR hilgers OR lightwire OR "light-wire" OR mbt OR mclaughin OR merrifield OR orthos OR "pre-programmed" OR ricketts OR roncone OR roth OR "Standard Edgewise" OR "Straight wire" OR straightwire OR "Tip-Edge" OR trevisi OR tweed OR "Tweed/Merrifield" OR "Variable Prescription Orthodontics") AND TITLE-ABS-KEY (random* OR blind*)) AND (LIMIT-TO (SUBJAREA , "DENT"))	Dentistry	101
Sum			290

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Appendix 3. List of included/excluded studies.

AA	PAPER	EXC
1	Alexander SA, Ripa LW. Effects of self-applied topical fluoride preparations in orthodontic patients. Angle Orthod 2000;70(6):424-30. Epub 2001/01/04.	Excluded by title
2	Baysal A, Uysal T, Ulker M, Usumez S. Effects of high-intensity curing lights on microleakage under bonded lingual retainers. Angle Orthod 2008;78(6):1084-8. Epub 2008/10/25.	Excluded by title
3	Boecler PR, Riolo ML, Keeling SD, TenHave TR. Skeletal changes associated with extraoral appliance therapy: an evaluation of 200 consecutively treated cases. Angle Orthod 1989;59(4):263-70. Epub 1989/01/01.	Excluded by title
4	Boyd RL. Longitudinal evaluation of a system for self-monitoring plaque control effectiveness in orthodontic patients. Journal of clinical periodontology. 1983;10(4):380-8. Epub 1983/07/01.	Excluded by title
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123	Cattaneo PM, Treccani M, Carlsson K, Thorgeirsson T, Myrda A, Cevidanes LH, et al. Transversal maxillary dento-alveolar changes in patients treated with active and passive self-ligating brackets: a randomized clinical trial using CBCT-scans and digital models. Orthodontics & craniofacial research. 2011;14(4):222-33. Epub 2011/10/20.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
124	Celar AG, Onodera K, Bertl MH, Astl E, Bantleon HP, Sato S, et al. Geometric morphometric evaluations of a randomized prospective split-mouth study on modes of ligation and reverse-curve mechanics. Orthodontics & craniofacial research. 2014;17(3):158-69.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
125	Celikoglu M, Bayram M, Nur M, Kilkis D. Mandibular changes during initial alignment with SmartClip self-ligating and conventional brackets: A single-center prospective randomized controlled clinical trial. Korean Journal of Orthodontics. 2015;45(2):89-94.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
126	Chen XH, Hua YM, Xie XQ, Yu XJ, Wang J, Liu LM. [Clinical study of extraction treatment of Class II division I malocclusion with Empower self-ligating brackets]. Shanghai kou qiang yi xue = Shanghai journal of stomatology. 2013;22(3):316-21. Epub 2013/07/16.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
127	Fleming PS, DiBiase AT, Sarri G, Lee RT. Comparison of mandibular arch changes during alignment and leveling with 2 preadjusted edgewise appliances. Am J Orthod Dentofac Orthop 2009;136(3):340-7.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
128	Fleming PS, DiBiase AT, Sarri G, Lee RT. Efficiency of mandibular arch alignment with 2 preadjusted edgewise appliances. Am J Orthod Dentofac Orthop 2009;135(5):597-602. Epub 2009/05/05.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
129	Fleming PS, Lee RT, Marinho V, Johal A. Comparison of maxillary arch dimensional changes with passive and active self-ligation and conventional brackets in the permanent dentition: a multicenter, randomized controlled trial. Am J Orthod Dentofac Orthop 2013;144(2):185-93. Epub 2013/08/06.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances

130	Fleming PS, Lee RT, McDonald T, Pandis N, Johal A. The timing of significant arch dimensional changes with fixed orthodontic appliances: data from a multicenter randomised controlled trial. Journal of dentistry. 2014;42(1):1-6. Epub 2013/11/26.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
131	Johansson K, Lundstrom F. Orthodontic treatment efficiency with self-ligating and conventional edgewise twin brackets: a prospective randomized clinical trial. Angle Orthod 2012;82(5):929-34. Epub 2012/03/09.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
132	O'Dywer L, Littlewood SJ, Rahman S, Spencer RJ, Barber SK, Russell JS. A multi-center randomized controlled trial to compare a self-ligating bracket with a conventional bracket in a UK population: Part 1: Treatment efficiency. Angle Orthodontist. 2016;86(1):142-8.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
133	Pandis N, Polychronopoulou A, Eliades T. Active or passive self-ligating brackets? A randomized controlled trial of comparative efficiency in resolving maxillary anterior crowding in adolescents. Am J Orthod Dentofac Orthop 2010;137(1):12 e1-6; discussion -3. Epub 2010/02/04.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
134	Pandis N, Polychronopoulou A, Eliades T. Self-ligating vs conventional brackets in the treatment of mandibular crowding: a prospective clinical trial of treatment duration and dental effects. Am J Orthod Dentofac Orthop 2007;132(2):208-15. Epub 2007/08/19.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
135	Pandis N, Strigou S, Eliades T. Maxillary incisor torque with conventional and self-ligating brackets: a prospective clinical trial. Orthodontics & craniofacial research. 2006;9(4):193-8. Epub 2006/11/15.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
136	Polat O, Gokcelik A, Arman A, Arhun N. A comparison of white spot lesion formation between a self-ligating bracket and a conventional preadjusted straight wire bracket. World journal of orthodontics. 2008;9(2):e46-50. Epub 2009/07/31.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
137	Rahman S, Spencer RJ, Littlewood SJ, O'Dywer L, Barber SK, Russell JS. A multicenter randomized controlled trial to compare a self-ligating bracket with a conventional bracket in a UK population: Part 2: Pain perception. Angle Orthodontist. 2016;86(1):149-56.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
138	Scott P, DiBiase AT, Sherriff M, Cobourne MT. Alignment efficiency of Damon3 self-ligating and conventional orthodontic bracket systems: a randomized clinical trial. Am J Orthod Dentofac Orthop 2008;134(4):470 e1-8. Epub 2008/10/22.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
139	Scott P, Sherriff M, DiBiase AT, Cobourne MT. Perception of discomfort during initial orthodontic tooth alignment using a self-ligating or conventional bracket system: a randomized clinical trial. Eur J Orthod 2008;30(3):227-32.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
140	Songra G, Clover M, Atack NE, Ewings P, Sherriff M, Sandy JR, et al. Comparative assessment of alignment efficiency and space closure of active and passive self-ligating vs conventional appliances in adolescents: a single-center randomized controlled trial. Am J Orthod Dentofac Orthop 2014;145(5):569-78. Epub 2014/05/03.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
141	Wahab RM, Idris H, Yacob H, Ariffin SH. Comparison of self- and conventional-ligating brackets in the alignment stage. Eur J Orthod 2012;34(2):176-81. Epub 2011/04/12.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
142	Wong H, Collins J, Tinsley D, Sandler J, Benson P. Does the bracket-ligature combination affect the amount of orthodontic space closure over three months? A randomized controlled trial. Journal of orthodontics. 2013;40(2):155-62. Epub 2013/06/26.	Excluded by fulltext; comparison between self- and conventionally-ligated appliances
143	Lotzof LP, Fine HA, Cisneros GJ. Canine retraction: a comparison of two preadjusted bracket systems. Am J Orthod Dentofac Orthop 1996;110(2):191-6. Epub 1996/08/01.	Excluded by fulltext; partial appliances used
144	Carcara S, Preston CB, Jureyda O. The relationship between the curve of Spee, relapse, and the Alexander Discipline. Seminars in Orthodontics. 2001;7(2):90-9.	Excluded by fulltext; non-randomized trial
145	Costopoulos G, Nanda R. An evaluation of root resorption incident to orthodontic intrusion. Am J Orthod Dentofac Orthop 1996;109(5):543-8. Epub 1996/05/01.	Excluded by fulltext; non-randomized trial
146	El-Angbawi AM, Bearn DR, McIntyre GT. Comparing the effectiveness of the 0.018-inch versus the 0.022-inch bracket slot system in orthodontic treatment: study protocol for a randomized controlled trial. Trials. 2014;15:389. Epub 2014/10/08.	Excluded by fulltext; ongoing trial
147	Altug-Atac AT, Erdem D, Arat ZM. Three-dimensional bimetric maxillary distalization arches compared with a modified Begg intraoral distalization system. Eur J Orthod 2008;30(1):73-9. Epub 2007/10/20.	Included

148	Reukers EA, Sanderink GC, Kuijpers-Jagtman AM, van't Hof MA. Radiographic evaluation of apical root resorption with 2 different types of edgewise appliances. Results of a randomized clinical trial. J Orofac Orthop 1998;59(2):100-9. Epub 1998/05/13.	Included
149	Sharma V, Sengupta J. Modifications to increase efficiency of the Begg orthodontic technique. Armed Forces medical journal, India 2009; (2):118-22.	Included
150	Talapaneni AK, Supraja G, Prasad M, Kommi PB. Comparison of sagittal and vertical dental changes during first phase of orthodontic treatment with MBT vs ROTH prescription. Indian journal of dental research : official publication of Indian Society for Dental Research. 2012;23(2):182-6. Epub 2012/09/05.	Included
151	Bhavra GS. A prospective RCT comparing Straight-Wire and Tip-. Edge fixed appliance systems. British Orthodontic Conference 2001 [abstract].	Included; unpublished trial coded as "O'Neil [unpublished]"
152	O'Neill J. Straight-Wire versus Tip-Edge: A randomized controlled trial. 32nd Meeting of the Annual Angle Society of Europe, Going, Austria.	Included; unpublished trial coded as "O'Neil [unpublished]"
153	Eslavath SN, Mood TN, Narahari KA, Chekka M, Natta S. Evaluation of treatment changes produced by different orthodontic treatment modalities using Peer Assessment Rating (PAR) index. J NTR Univ Health Sci 2015;4:97-102.	Judgement pending; trial possibly eligible; trialists contacted for clarification
154	Carmona Lorduy M, Vergara CI. Asociacion de diferentes tecnicas de ortodoncia fija con la aparicion de lesiones orales sobre tejidos blandos. Universidad de Cartagena, Facultad de Odontologìa, 2016.	Judgement pending; trial possibly eligible; trialists contacted for clarification
155	Pacheco Orellana CA. Cambios corticales en los dientes anteriores superiores e inferiores con brackets convencionales, Damon y Biofuncional QR en pacientes de trece a veinte y cuatro años. Universidad de Cuenca, 2016.	Judgement pending; trial possibly eligible; trialists contacted for clarification
156	Rajesh M, Kishore MS, Shetty KS. Comparison of anchorage loss following initial leveling and aligning using ROTH and MBT Prescription – A clinical prospective study. J Int Oral Health 2014;6(2):16-21.	Judgement pending; trial possibly eligible; trialists contacted for clarification
157	Ruiz Reascos PE. Reabsorción radicular externa apical en incisivos y caninos superiores e inferiores sometidos a tratamiento de Ortodoncia en etapa inicial.	Judgement pending; trial possibly eligible; trialists contacted for clarification

Appendix 4. Detailed risk of bias assessment for the included trials.

AA	Trial	Sequence generation	Allocation concealment	Blinding of participants/ personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias
1	Altug-Atac 2008	**Unclear** – "The subjects were randomly selected from among those referred to the Department of Orthodontics…".	**Unclear** – No mention throughout the paper.	**Unclear** - Blinding is impractical for both patients and clinician; outcome is objective, but was not assessed blindly.	**High risk** - no mention of blinding throughout the paper; blinding could have been implemented.	**High risk –** High drop out rate (24%) resulting in imbalance of the compared groups; no formal method has been used to take care of attrition bias.	**Unclear** – It is difficult to judge whether selective reporting is a problem, as no protocol exists.	**Unclear** - residual bias cannot be excluded.
2	O'Neil unpublished	**Unclear** – "Separate randomisation was carried out for males and females. Randomisation was carried out using the process described by Pocock (1983)."	**Low risk** – central allocation: "The randomisation procedure was performed by a statistician not involved in the clinical trial"	**Low risk** - Blinding is impractical for both patients and clinician; outcome is objective and was assessed blindly.	**Low risk** - Blinding of outcome assessors: "An independent calibrated technician undertook weighted PAR assessments, blinded to the appliance system used, for the pre and post treatment models."	**Unclear –** A drop-out rate of about 18% was reported (73 patients completed from the 89 randomized). No information about a potential group imbalance according to patient characteristics or an imputation technique is provided, although the final samples in each group are similar (35 and 38).	**Low risk** – No trial registration or protocol is available. However, the authors report detailed deviations from protocol for each potential outcome.	**Unclear** - residual bias cannot be excluded.
3	Reukers 1997;1998	**Low risk** - "The type of treatment was randomly assigned by a computer program."	**Low risk** – central allocation: "When the treatment modality was assigned, the orthodontist was informed by the secretary of the central trial registration what treatment was to be used for that patient".	**Low risk** - Blinding is impractical for both patients and clinician; outcome is objective and was assessed blindly.	**Low risk** - Blinding of outcome assessors: "Blinding the evaluators could be performed in all instances… every record that had to be evaluated in such a way that the evaluator could not recognize name of the patient, treatment option and/or the practice were treatment took place."	**Unclear -** The evaluation of apical root resorption was based on only 61 out of the 149 randomized patients. The authors report that "This selection will, however, not introduce a selection bias in the comparison of FPA versus PPA", but no formal assessment of the patients' baseline characteristics or treatment modalities and co-interventions is undertaken, to ascert that they were representative. As for the rest investigated variables no clear judgement can be made, as no further description about the allocation of the drop-outs is given and no adjustment is made in the analysis.	**Low risk** – trial protocol registered and fully reported outcomes that the trial was based upon.	**Unclear** - residual bias cannot be excluded.

4	Sharma 2009	**Unclear** – "Thirty patients each were randomly assigned for treatment with one of the three fixed appliance techniques."	**Unclear** – No mention throughout the paper.	**Unclear** - Blinding is impractical for both patients and clinician; outcome is objective, but was not assessed blindly.	**High risk** - no mention of blinding throughout the paper; blinding could have been implemented.	**Low risk** - No drop-outs or patient losses are reported.	**Unclear** - It is difficult to judge whether selective reporting is a problem, as no protocol exists.	**Unclear** - residual bias cannot be excluded.
5	Talapaneni 2012	**Unclear** – randomization description inadequate: "..subjects who were randomly divided into two Groups"	**Unclear** – No mention throughout the paper.	**Unclear** - Blinding is impractical for both patients and clinician; outcome is objective, but was not assessed blindly.	**High risk** - no mention of blinding throughout the paper; blinding could have been implemented.	**Low risk** - No drop-outs or patient losses are reported.	**Unclear** - It is difficult to judge whether selective reporting is a problem, as no protocol exists.	**Unclear** - residual bias cannot be excluded.

Appendix 5. Details about the GRADE assessment regarding the comparison of a Roth versus Begg /modified technique for the fixed orthodontic appliance.

Outcomes	Roth vs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication bias	Large Effect	Dose Response	Residual Confounding
Total chairtime (in minutes)	Begg	Starts from "high", due to the inclusion of randomized studies. Downgraded by one due to bias.	Not assessed.	Directly relevant.	No reason to downgrade.	Not assessed.	No reason to upgrade.	No reason to upgrade.	No reason to upgrade.
Total chairtime (in minutes)	Mod. Begg	Same as above.	Same as above.	Same as above.	No reason to downgrade.	Same as above.	Same as above.	Same as above.	Same as above.
Occlusal outcome (final PAR)	Begg	Same as above.	Same as above.	Same as above.	Downgraded by one for imprecision due to small sample size.	Same as above.	Same as above.	Same as above.	Same as above.
Occlusal outcome (final PAR)	Mod. Begg	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.
Upper incisor inclination (1s-SN change in °)	Begg	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.
Upper incisor inclination (1s-SN change in °)	Mod. Begg	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.
Lower incisor inclination (1s-SN change in °)	Begg	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.
Lower incisor inclination (1s-SN change in °)	Mod. Begg	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.

Mod., modified; PAR, peer assessment rating.

Appendix 6. Details about the GRADE assessment regarding the comparison of a fully versus a partially programmed fixed orthodontic appliance.

	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication bias	Large Effect	Dose Response	Residual Confounding
Tx duration (in months)	Starts from "high", due to the inclusion of randomized studies. No reason to downgrade.	Not assessed.	Directly relevant.	No reason to downgrade.	Not assessed.	No reason to upgrade.	No reason to upgrade.	No reason to upgrade.
Occlusal outcome (% reduction of initial PAR score)	Same as above.	Same as above.	Same as above.	No reason to downgrade. Effect crosses the line of no effect, but also excludes important benefit/effects.	Same as above.	Same as above.	Same as above.	Same as above.
Upper incisor inclination (final 1s-NL in °)	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.
Lower incisor inclination (final 1i-ML in °)	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.
Prevalence of root resorption	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.	Same as above.

Tx, treatment; PAR, peer assessment rating.

Appendix 7. Details of communications with trialist performed for this systematic review.

Nr	Citation	Contact	Status
1	Eslavath SN, Mood TN, Narahari KA, Chekka M, Natta S. Evaluation of treatment changes produced by different orthodontic treatment modalities using Peer Assessment Rating (PAR) index. J NTR Univ Health Sci 2015;4:97-102.	E. Seena Naik	Sent 8.8.16
2	Carmona Lorduy M, Vergara CI. Asociacion de diferentes tecnicas de ortodoncia fija con la aparicion de lesiones orales sobre tejidos blandos. Universidad de Cartagena, Facultad de Odontologìa, 2016.	Martha Camona Lorduy	Sent 8.8.16
3	Pacheco Orellana CA. Cambios corticales en los dientes anteriores superiores e inferiores con brackets convencionales, Damon y Biofuncional QR en pacientes de trece a veinte y cuatro años. Universidad de Cuenca, 2016.	E-mail could not be found	Sent 8.8.16
4	Rajesh M, Kishore MS, Shetty KS. Comparison of anchorage loss following initial leveling and aligning using ROTH and MBT Prescription – A clinical prospective study. J Int Oral Health 2014;6(2):16-21.	Rajesh M	Sent 8.8.16
5	Ruiz Reascos PE. Reabsorción radicular externa apical en incisivos y caninos superiores e inferiores sometidos a tratamiento de Ortodoncia en etapa inicial	Diego Mauricio Bravo Calderón	Sent 8.8.16
6	Sharma V, Sengupta J. Modifications to increase efficiency of the Begg orthodontic technique. Armed Forces medical journal, India 2009; (2):118-22.	Vineet Sharma	Sent 30.8.16
7	Bhavra GS. A prospective RCT comparing Straight-Wire and Tip-. Edge fixed appliance systems. British Orthodontic Conference 2001 [abstract].	Julian O'Neill	Answered; provided unpublished trial report
8	O'Neill J. Straight-Wire versus Tip-Edge: A randomized controlled trial. 32nd Meeting of the Annual Angle Society of Europe, Going, Austria.		

Appendix 8. Changes to the protocol

- The number needed to treat was planned to be used to clinically translate the results of statistically significant meta-analyses of binary outcomes, but only limited statistical analyses were included and no statistically significant binary meta-analyses.
- Between-trial heterogeneity was planned to be quantified with the I^2 statistic, defined as the proportion of total variability in the results explained by heterogeneity, and not chance [Higgins et al., 2003]. The 95% uncertainty intervals (95% UI) (similar to CIs) around the I2 were planned to be calculated [Ioannidis et al., 2007] using the non-central $\chi 2$ approximation of Q [Orsini et al., 2006]. 95% predictive intervals were planned to be calculated for meta-analyses of three trials or more, which incorporate existing heterogeneity and provide a range of possible effects for a future clinical setting [Inhout et al., 2016]. All these were not performed due to the limited number of included studies.
- Possible sources of heterogeneity were planned to be sought through pre-specified mixed-effects subgroup analyses and random-effects meta-regression with the Knapp and Hartung [2003] adjustment in meta-analyses of at least five trials. A two-tailed P-value of 0.10 was to be considered significant for the test of heterogeneity and reporting biases, due to low power [Ioannidis, 2008]. Indications of reporting biases (including small-study effects) were planned to be assessed with Egger's linear regression test [Egger et al., 1997] and contour-enhanced funnel plots, should ten or more trials be pooled. Robustness of the results was planned a priori to be checked with sensitivity analyses, if at least three trials were pooled on a MA. All these were not performed due to the limited number of included studies.
- The produced forest plots were to be augmented with contours denoting the magnitude of the observed effect, but this was omitted, as no meta-analyses were performed and therefore no forest plots were constructed.